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FILE LAST UPDATED: 24 Apr 2008 (20080424/ED)

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=> s anti-acetylated histone antibody
      494258 ANTI
          12 ANTIS
      494266 ANTI
                (ANTI OR ANTIS)
       32645 ACETYLATED
       36549 HISTONE
       27207 HISTONES
       42243 HISTONE
                (HISTONE OR HISTONES)
      328345 ANTIBODY
      392837 ANTIBODIES
      521022 ANTIBODY
                (ANTIBODY OR ANTIBODIES)
L1          3 ANTI-ACETYLATED HISTONE ANTIBODY
                (ANTI(W)ACETYLATED(W)HISTONE(W)ANTIBODY)

=> duplicate remove L1
PROCESSING COMPLETED FOR L1
L2          3 DUPLICATE REMOVE L1 (0 DUPLICATES REMOVED)

=> d L2 bib abs 1-3

L2  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2008 ACS on STN
AN  2004:266919  CAPLUS
DN  140:281367
TI  Antibody tools for the diagnostic use in the medical therapy with
    inhibitors of histone deacetylases
IN  Pelicci, Pier Giuseppe; Minucci, Saverio; Piccini, Daniele; Maccarana,
    Marco; Ronzoni, Simona; Areces, Liliana Beatriz; Faretta, Marco
PA  G2m Cancer Drugs Ag, Germany
SO  Eur. Pat. Appl., 36 pp.
    CODEN: EPXXDW
DT  Patent
LA  English
FAN.CNT 1
    PATENT NO.         KIND   DATE       APPLICATION NO.      DATE
    ---------------    ----   --------   -------------------  --------
PI  EP 1403639         A1     20040331   EP 2002-21984        20020930
      R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
         IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
    CA 2500384         A1     20040408   CA 2003-2500384      20030930
    WO 2004029622      A2     20040408   WO 2003-EP10842      20030930
    WO 2004029622      A3     20040805
      W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003271663 A1 20040419 AU 2003-271663 20030930
EP 1546712 A2 20050629 EP 2003-753482 20030930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2006501279 T 20060112 JP 2004-539052 20030930
US 20060257948 A1 20061116 US 2005-529792 20051110
PRAI EP 2002-21984 A 20020930
WO 2003-EP10842 W 20030930
AB The invention relates to a method for detg. whether a treatment of a disorder with an histone deacetylases (HDAC) inhibitor is to be started/continued or not comprising detg. the level of histone acetylation in the sample by use of an antibody capable of binding to acetylated histone, and classifying the disorder as to be treated with an HDAC inhibitor when the level of histone acetylation is significantly lower than that of a ref. sample. The invention further relates to the diagnostic and prognostic use of specific antibodies and cell lines producing them.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2002:430579 CAPLUS
DN 137:153179
TI Chromatin disruption and histone acetylation in regulation of the human immunodeficiency virus type 1 long terminal repeat by thyroid hormone receptor
AU Hsia, Shao-Chung Victor; Shi, Yun-Bo
CS Unit on Molecular Morphogenesis, Laboratory of Gene Regulation and Development, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, 20892-5431, USA
SO Molecular and Cellular Biology (2002), 22(12), 4043-4052
CODEN: MCEBD4; ISSN: 0270-7306
PB American Society for Microbiology
DT Journal
LA English
AB The human immunodeficiency virus type 1 (HIV-1) long terminal repeat (LTR)

controls the expression of HIV-1 viral genes and thus viral propagation and pathol. Numerous host factors participate in the regulation of the LTR promoter, including thyroid hormone (T3) receptor (TR). In vitro, TR can bind to the promoter region contg. the NF-.kappa.B and Sp1 binding sites. Using the frog oocyte as a model system for chromatin assembly mimicking that in somatic cells, we demonstrated that TR alone and TR/RXR (9-cis retinoic acid receptor) can bind to the LTR in vivo independently of T3. Consistent with their ability to bind the LTR, both TR and TR/RXR can regulate LTR activity in vivo. In addn., our anal. of the plasmid minichromosome shows that T3-bound TR disrupts the normal nucleosomal array structure. Chromatin immunopptn. assays with anti-acetylated-histone antibodies revealed that unliganded TR and TR/RXR reduce the local histone acetylation levels at the HIV-1 LTR while T3 treatment reverses this redn. We further demonstrated that unliganded TR recruits corepressors and at least one histone deacetylase. These results suggest that chromatin remodeling, including histone acetylation and chromatin disruption, is important for T3 regulation of the HIV-1 LTR in vivo.

RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:619539 CAPLUS

DN 137:292558

TI Transcriptional deregulation of the keratin 18 gene in human colon carcinoma cells results from an altered acetylation mechanism

AU Prochasson, Philippe; Delouis, Cecile; Brison, Olivier

CS Laboratoire de Genetique Oncologique, UMR 1599 CNRS, Institut Gustave-Roussy, Villejuif, 94805, Fr.

SO Nucleic Acids Research (2002), 30(15), 3312-3322
CODEN: NARHAD; ISSN: 0305-1048

PB Oxford University Press

DT Journal

LA English

AB The authors are investigating the mechanism responsible for the overexpression of the keratin 18 (K18) gene in tumorigenic clones from the SW613-S human colon carcinoma cell line, as compared with non-tumorigenic clones. The authors have previously shown that this mechanism affects the minimal K18 promoter (TATA box and initiation site). The authors report here that treatment of the cells with histone deacetylase inhibitors stimulates the activity of the promoter in non-tumorigenic cells but has no effect in tumorigenic cells, resulting in a comparable activity of the promoter in both cell types. The adenovirus E1A protein inhibits the activity of the K18 promoter specifically in tumorigenic cells. This inhibition can be reversed by an excess of CBP protein. The conserved

region 1 (CR1) of E1A, which is involved in the interaction with the CBP/p300 co-activators, is necessary to the inhibitory capacity of E1A. A 79 amino acid long N-terminal fragment of E1A, encompassing the two domains of E1A necessary and sufficient for binding to CBP (N-terminus and CR1), has the same differential inhibitory capacity on the K18 promoter as wild-type E1A. Forced recruitment of GAL4-CBP fusion proteins to the K18 promoter results in a greater stimulation of its activity in non-tumorigenic than in tumorigenic cells. The histone acetyltransferase activity of CBP is essential for this differential stimulation and the presence of the CBP2 domain greatly augments the activation capacity of the fusion protein. Chromatin immunopptn. expts. carried out with anti-acetylated histone antibodies showed no difference in the level of histone acetylation in the region of the K18 promoter between the two cell types. The structure of chromatin in the promoter region is similar in tumorigenic and non-tumorigenic cells, as detd. by mapping of DNase I hypersensitive sites and probing the accessibility of the DNA to restriction endonucleases. From all these results the authors conclude that alteration of an acetylation mechanism involving the CBP (or p300) protein and acting on a non-histone substrate is responsible for the higher activity of the K18 promoter in tumorigenic cells of the SW613-S cell line.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s acetylated histone H4 and antibody

32645 ACETYLATED
36549 HISTONE
27207 HISTONES
42243 HISTONE
(HISTONE OR HISTONES)
10699 H4
134 ACETYLATED HISTONE H4
(ACETYLATED(W)HISTONE(W)H4)
328345 ANTIBODY
392837 ANTIBODIES
521022 ANTIBODY
(ANTIBODY OR ANTIBODIES)

L3 36 ACETYLATED HISTONE H4 AND ANTIBODY

=> duplicate remove L3

PROCESSING COMPLETED FOR L3

L4 36 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> L4 and HDAC

L4 IS NOT A RECOGNIZED COMMAND
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For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s L4 and HDAC
L5 36 S L4
2518 HDAC
965 HDACS
2819 HDAC
(HDAC OR HDACS)
L6 4 L5 AND HDAC

=> duplicate remove L6
PROCESSING COMPLETED FOR L6
L7 4 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)

=> d L7 bib abs 1-4

L7 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:266919 CAPLUS
DN 140:281367
TI Antibody tools for the diagnostic use in the medical therapy
with inhibitors of histone deacetylases
IN Pelicci, Pier Giuseppe; Minucci, Saverio; Piccini, Daniele; Maccarana,
Marco; Ronzoni, Simona; Areces, Liliana Beatriz; Faretta, Marco
PA G2m Cancer Drugs Ag, Germany
SO Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1403639	A1	20040331	EP 2002-21984	20020930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CA 2500384	A1	20040408	CA 2003-2500384	20030930
WO 2004029622	A2	20040408	WO 2003-EP10842	20030930
WO 2004029622	A3	20040805		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003271663 A1 20040419 AU 2003-271663 20030930

EP 1546712 A2 20050629 EP 2003-753482 20030930

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2006501279 T 20060112 JP 2004-539052 20030930

US 20060257948 A1 20061116 US 2005-529792 20051110

PRAI EP 2002-21984 A 20020930

WO 2003-EP10842 W 20030930

AB The invention relates to a method for detg. whether a treatment of a disorder with an histone deacetylases (HDAC) inhibitor is to be started/continued or not comprising detg. the level of histone acetylation in the sample by use of an antibody capable of binding to acetylated histone, and classifying the disorder as to be treated with an HDAC inhibitor when the level of histone acetylation is significantly lower than that of a ref. sample. The invention further relates to the diagnostic and prognostic use of specific antibodies and cell lines producing them.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:640399 CAPLUS

DN 142:49040

TI The activity of antiepileptic drugs as histone deacetylase inhibitors

AU Eyal, Sara; Yagen, Boris; Sobol, Eyal; Altschuler, Yoram; Shmuel, Miriam; Bialer, Meir

CS Department of Pharmaceutics, School of Pharmacy, Faculty of Medicine, Hebrew University of Jerusalem, Israel

SO Epilepsia (2004), 45(7), 737-744

CODEN: EPILAK; ISSN: 0013-9580

PB Blackwell Publishing, Inc.

DT Journal

LA English

AB Purpose: Valproic acid (VPA), one of the widely used antiepileptic drugs (AEDs), was recently found to inhibit histone deacetylases (HDACs). HDAC inhibitors of a wide range of structures, such as hydroxamic acids, carboxylic acids, and cyclic tetrapeptides, have various effects on transformed and nontransformed cells, including neuromodulation and neuroprotection. The aim of this study was to assess comparatively the activity of traditional and newer AEDs as HDAC inhibitors. Methods: After incubation of HeLa cells with the tested AEDs, histone

hyperacetylation was assessed by immunoblotting with an antibody specific to acetylated histone H4. Direct HDAC inhibition by AEDs was estd. by using HeLa nuclear ext. as an HDACs source and an acetylated lysine substrate. Results: We found that in addn. to VPA, topiramate (TPM) inhibited HDACs with apparent Ki values of 2.22 .+-. 0.67 mM. Although levetiracetam (LEV) had no direct effect on HDACs, its major carboxylic acid metabolite in humans, 2-pyrrolidinone-n-butyric acid (PBA), inhibited HDACs with Ki values of 2.25 .+-. 0.78 mM. The AEDs LEV, phenobarbital, phenytoin, carbamazepine, ethosuximide, gabapentin, and vigabatrin did not inhibit HDACs. The compds. that directly inhibited HDACs also induced the accumulation of acetylated histone H4 in HeLa cells. The effects of TPM and PBA on histone acetylation were significant at 0.25 mM and 1 mM, resp. Conclusions: We found that in addn. to VPA, the newer AED TPM and the major metabolite of LEV, PBA, are able to induce histone hyperacetylation in human cells, although with lower potencies than VPA.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:83868 CAPLUS

DN 138:253482

TI The effect of oxidative stress on histone acetylation and IL-8 release

AU Tomita, K.; Barnes, P. J.; Adcock, I. M.

CS Thoracic Medicine, Imperial College School of Science, Technology and Medicine, National Heart and Lung Institute, London, SW3 6LY, UK

SO Biochemical and Biophysical Research Communications (2003), 301(2), 572-577
CODEN: BBRCA9; ISSN: 0006-291X

PB Elsevier Science

DT Journal

LA English

AB Acetylation of histone residues regulates the expression of inflammatory genes and is controlled by the activities of histone acetyltransferases (HAT) and histone deacetylases (HDAC). Anal. of histone acetylation in human cells is limited by the large nos. needed to perform activity assays or Western blotting. We have used flow cytometry to investigate changes in HAT and HDAC activities at the single cell level and to investigate the effect of hydrogen peroxide (H2O2) on histone H4 acetylation and cell-cycle progression. Using an anti-acetylated histone H4 antibody we show that H2O2 induced a time-dependent increase in histone acetylation that was maintained for 12 h. This was assocd. with increased IL-8 prodn. H2O2 also affected cell-cycle progression. HAT activity was found to be

highest in G2/M and equiv. in G0/G1 and S phases of the cell cycle. These data show that detection of acetylated histone residues at the single cell level using FACs may be a powerful new tool for the anal. of modulation of cell proliferation and gene transcription.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:868228 CAPLUS

DN 138:362277

TI Inhibitors of histone deacetylase and DNA methyltransferase synergistically activate the methylated metallothionein I promoter by activating the transcription factor MTF-1 and forming an open chromatin structure

AU Ghoshal, Kalpana; Datta, Jharna; Majumder, Sarmila; Bai, Shoumei; Dong, Xiaocheng; Parthun, Mark; Jacob, Samson T.

CS Department of Molecular and Cellular Biochemistry, College of Medicine, The Ohio State University, Columbus, OH, 43210, USA

SO Molecular and Cellular Biology (2002), 22(23), 8302-8319
CODEN: MCEBD4; ISSN: 0270-7306

PB American Society for Microbiology

DT Journal

LA English

AB Inhibitors of DNA methyltransferase (Dnmt) and histone deacetylases (HDAC) synergistically activate the methylated metallothionein I gene (MT-I) promoter in mouse lymphosarcoma cells. The cooperative effect of these two classes of inhibitors on MT-I promoter activity was robust following demethylation of only a few CpG dinucleotides by brief exposure to 5-azacytidine (5-AzaC) but persisted even after prolonged treatment with the nucleoside analog. HDAC inhibitors (trichostatin A [TSA] and depsipeptide) either alone or in combination with 5-AzaC did not facilitate demethylation of the MT-I promoter. Treatment of cells with HDAC inhibitors increased accumulation of multiply acetylated forms of H3 and H4 histones that remained unaffected after treatment with 5-AzaC. Chromatin immunopptn. (ChIP) assay showed increased assocn. of acetylated histone H4 and lysine 9 (K9)-acetyl H3 with the MT-I promoter after treatment with TSA, which was not affected following treatment with 5-AzaC. In contrast, the assocn. of K9-Me histone H3 with the MT-I promoter decreased significantly after treatment with 5-AzaC and TSA. ChIP assay with antibodies specific for methyl-CpG binding proteins (MBDs) demonstrated that only methyl-CpG binding protein 2 (MeCP2) was assocd. with the MT-I promoter, which was significantly enhanced after TSA treatment. Assocn. of histone deacetylase 1 (HDAC1) with the promoter decreased after treatment with TSA or 5-AzaC and was abolished after treatment with both inhibitors. Among

the DNA methyltransferases, both Dnmt1 and Dnmt3a were assocd. with the MT-I promoter in the lymphosarcoma cells, and assocn. of Dnmt1 decreased with time after treatment with 5-AzaC. Treatment of these cells with HDAC inhibitors also increased expression of the MTF-1 (metal transcription factor-1) gene as well as its DNA binding activity. In vivo genomic footprinting studies demonstrated increased occupancy of MTF-1 to metal response elements of the MT-I promoter after treatment with both inhibitors. Anal. of the promoter by mapping with restriction enzymes in vivo showed that the MT-I promoter attained a more open chromatin structure after combined treatment with 5-AzaC and TSA as opposed to treatment with either agent alone. These results implicate involvement of multifarious factors including modified histones, MBDs, and Dnmts in silencing the methylated MT-I promoter in lymphosarcoma cells. The synergistic activation of this promoter by these two types of inhibitors is due to demethylation of the promoter and altered assocn. of different factors that leads to reorganization of the chromatin and the resultant increase in accessibility of the promoter to the activated transcription factor MTF-1.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s histone acetylation and antibody

36549 HISTONE
27207 HISTONES
42243 HISTONE
(HISTONE OR HISTONES)
72076 ACETYLATION
281 ACETYLATIONS
72150 ACETYLATION
(ACETYLATION OR ACETYLATIONS)
2939 HISTONE ACETYLATION
(HISTONE(W)ACETYLATION)
328345 ANTIBODY
392837 ANTIBODIES
521022 ANTIBODY
(ANTIBODY OR ANTIBODIES)

L8 154 HISTONE ACETYLATION AND ANTIBODY

=> s L8 and HDAC

2518 HDAC
965 HDACS
2819 HDAC
(HDAC OR HDACS)

L9 19 L8 AND HDAC

=> s L9 and H4
10699 H4
L10 12 L9 AND H4

=> d L10 bib abs 1-12

L10 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:584090 CAPLUS
DN 145:227886
TI Histone deacetylation is required for orderly meiosis
AU Wang, Qiang; Yin, Shen; Ai, Jun-Shu; Liang, Cheng-Guang; Hou, Yi; Chen, Da-Yuan; Schatten, Heide; Sun, Qing-Yuan
CS State Key Laboratory of Reproductive Biology; Institute of Zoology, Chinese Academy of Sciences, Beijing, Peop. Rep. China
SO Cell Cycle (2006), 5(7), 766-774
CODEN: CCEYAS; ISSN: 1538-4101
PB Landes Bioscience
DT Journal
LA English
AB We first investigated in detail the acetylation changes during porcine oocyte maturation using a panel of antibodies specific for the crit. acetylated forms of histone H3 and H4, and showed meiosis stage-dependent and lysine residue-specific patterns of histone acetylation. By using trichostatin A (TSA), a general inhibitor of histone deacetylases (HDACs), we further detd. that selective inhibition of histone deacetylation (thereby maintaining hyperacetylation) delayed the onset of germinal vesicle breakdown and produced a high frequency of lagging chromosomes or chromatin bridges at anaphase and telophase I (AT-I), suggesting that histone deacetylation is required for orderly meiotic resumption and accurate chromosome segregation in porcine oocytes. In addn., we examd. the localization and expression of HDAC1 by performing immunofluorescence and immunoblotting anal. Subcellular translocation, expression level, and phosphorylated modification of HDAC1 were temporally regulated and likely to coparticipate in the establishment of histone acetylation profiles in oocyte meiosis.
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:40472 CAPLUS
DN 144:367459
TI Epigenetic activation of .alpha.4, .beta.2 and .beta.6 integrins involved in cell migration in trichostatin A-treated Hep3B cells
AU Lin, Kuen-Tyng; Yeh, Shiou-Hwei; Chen, Ding-Shinn; Chen, Pei-Jer; Jou,

Yuh-Shan
CS Graduate Institute of Life Sciences, National Defense Medical Center, National Defense University, Taipei, Taiwan
SO Journal of Biomedical Science (Dordrecht, Netherlands) (2005), 12(5), 803-813
CODEN: JBCIEA; ISSN: 1021-7770
PB Springer
DT Journal
LA English
AB The epigenetic modulation by histone deacetylase (HDAC) inhibitors including trichostatin A (TSA) has been known to block cell proliferation, induce apoptosis and inhibit cell migration in human cancer cells that represents the potential therapeutic agents for cancers and fibrosis. However, more than 55% of Hep3B cells remained alive after our initial study of 100 nM TSA treatment. To further study the epigenetic modulation and the biol. function of newly activated genes by HDAC inhibitor involved in HCC progression and metastasis, we profiled 23 integrin genes including 15.alpha. and 8.beta. in TSA-treated Hep3B cells. Six integrins including three down-regulated .alpha.6, .alpha.10, .beta.8 and three significant up-regulated .alpha.4, .beta.2, .beta.6 integrins were revealed after semi-quant. RT-PCR. To confirm the epigenetic modulation and explore their biol. functions, we selected the three significantly up-regulated integrins for confirmation of protein up-regulation, hyperacetylated-histones by ChIP assays, and functional inhibition by specific neutralizing antibodies of integrins. Our results indicated that epigenetic modulation in TSA-treated Hep3B cells up-regulated new integrins including .alpha.4, .beta.2 and .beta.6 and reduced migration activities by specific neutralizing antibodies to 61.3%, 42.4% and 34.5%, resp. Our novel findings provided a better understanding of the epigenetic modulation of integrins and suggested that targeting the epigenetic up-regulated integrins to abrogate the migration activity might be a promising strategy to prevent HCC progression.
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:642598 CAPLUS
DN 144:208314
TI New method to detect histone acetylation levels by flow cytometry
AU Ronzoni, Simona; Faretta, Mario; Ballarini, Marco; Pelicci, PierGiuseppe; Minucci, Saverio
CS European Institute of Oncology, Milan, Italy
SO Cytometry, Part A (2005), 66A(1), 52-61

CODEN: CPAYAV; ISSN: 1552-4922
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Background: Reversible histone acetylation affects chromatin structural organization, thus regulating gene expression and other nuclear events. Levels of histone acetylation are tightly modulated in normal cells, and alterations of their regulating mechanisms have been shown to be involved in tumorigenesis. Methods: the authors developed a new flow cytometric technique for detection of histone acetylation, based on a specific monoclonal antibody that recognizes acetylated histone tails. Bivariate anal. for histone acetylation levels and DNA were performed to study modulation of chromatin organization during the cell cycle and after induction of histone hyperacetylation by the histone deacetylase (HDAC) inhibitor trichostatin A (TSA). Histone acetylation and transcription levels were monitored during differentiation induced by retinoic acid alone or in combination with TSA. Blood samples from patients were analyzed with the described protocol to monitor the effects of HDAC inhibitors in vivo and validate the developed protocol for clin. usage. Results: Flow cytometric detection of acetylation status can successfully detect modifications induced by HDAC inhibitor treatment in vivo as demonstrated by anal. of various blood samples from patients treated with valproic acid. Changes in acetylation levels during the cell cycle demonstrated a reproducible increase in histone acetylation during the replication phase that was subsequently decreased at the G2M entrance, thus paralleling the behavior of DNA replication and transcriptional activity. Conclusions: Multiparameter anal. of histone acetylation and expression of mol. markers, DNA ploidy, and/or cell cycle kinetics can provide a quick and statistically reliable tool for the diagnosis and evaluation of treatment efficacy in clin. trials using HDAC inhibitors.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:19413 CAPLUS
DN 142:351883
TI BAF53/arp4 homolog Alp5 in fission yeast is required for histone H4 acetylation, kinetochore-spindle attachment, and gene silencing at centromere
AU Minoda, Aki; Saitoh, Shigeaki; Takahashi, Kohta; Toda, Takashi
CS Laboratory of Cell Regulation, London Research Institute, Lincoln's Inn Fields Laboratories, Cancer Research UK, London, WC2A 3PX, UK

SO Molecular Biology of the Cell (2004), Volume Date 2005, 16(1), 316-327
CODEN: MBCEEV; ISSN: 1059-1524
PB American Society for Cell Biology
DT Journal
LA English
AB Nuclear actin-related proteins play vital roles in transcriptional regulation; however, their biol. roles remain elusive. Here, we characterize Alp5, fission yeast homolog of Arp4/BAF53. The temp.-sensitive mutant alp5-1134 contains a single amino acid substitution in the conserved C-terminal domain (S402N) and displays mitotic phenotypes, including chromosome condensation and missegregation. Alp5 forms a complex with Mst1-HAT (histone acetyltransferase). Consistently, inhibition of histone deacetylases (HDACs), by either addn. of a specific inhibitor or a mutation in HDAC-encoding clr6+ gene, rescues alp5-1134. Immunoblotting with specific antibodies against acetylated histones shows that Alp5 is required for histone H4 acetylation at lysines 5, 8, and 12, but not histone H3 lysines 9 or 14, and furthermore Clr6 plays an opposing role. Mitotic arrest is ascribable to activation of the Mad2/Bub1 spindle checkpoint, in which both proteins localize to the mitotic kinetochores in alp5-1134. Intriguingly, alp5-1134 displays transcriptional desilencing at the core centromere without altering the overall chromatin structure, which also is suppressed by a simultaneous mutation in clr6+. This result shows that Alp5 is essential for histone H4 acetylation, and its crucial role lies in the establishment of bipolar attachment of the kinetochore to the spindle and transcriptional silencing at the centromere.
RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:746417 CAPLUS
DN 141:240597
TI Regulation of histone acetylation during meiotic maturation in mouse oocytes
AU Akiyama, Tomohiko; Kim, Jin-Moon; Nagata, Masao; Aoki, Fugaku
CS Department of Integrated Biosciences, Graduate School of Frontier Sciences, University of Tokyo, Chiba, Japan
SO Molecular Reproduction and Development (2004), 69(2), 222-227
CODEN: MREDEE; ISSN: 1040-452X
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Histone acetylation is an important epigenetic modification implicated in the regulation of chromatin structure and, subsequently, gene expression. Global histone deacetylation was reported

in mouse oocytes during meiosis but not mitosis. The regulation of this meiosis-specific deacetylation has not been elucidated. Here, we demonstrate that p34cdc2 kinase activity and protein synthesis are responsible for the activation of histone deacetylases and the inhibition of histone acetyltransferases (HATs), resp., resulting in deacetylation of histone H4 at lysine-12 (H4K12) during mouse oocyte meiosis. Temporal changes in the acetylation state of H4K12 were examd. immunocytochem. during meiotic maturation using an antibody specific for acetylated H4K12. H4K12 was deacetylated during the first meiosis, temporarily acetylated around the time of the first polar body (PB1) extrusion, and then deacetylated again during the second meiosis. Because these changes coincided with the known oscillation pattern of p34cdc2 kinase activity, we investigated the involvement of the kinase in H4K12 deacetylation. Roscovitine, an inhibitor of cyclin-dependent kinase activity, prevented H4K12 deacetylation during both the first and second meiosis, suggesting that p34cdc2 kinase activity is required for deacetylation during meiosis. In addn., cycloheximide, a protein synthesis inhibitor, also prevented deacetylation. After PB1 extrusion, at which time H4K12 had been deacetylated, H4K12 was re-acetylated in the condensed chromosomes by treatment with cycloheximide but not with roscovitine. These results demonstrate that HATs are present but inactivated by newly synthesized protein(s) that is (are) not involved in p34cdc2 kinase activity. Our results suggest that p34cdc2 kinase activity induces the deacetylation of H4K12 and that the deacetylated state is maintained by newly synthesized protein(s) that inhibits HAT activity during meiosis.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:640399 CAPLUS
DN 142:49040
TI The activity of antiepileptic drugs as histone deacetylase inhibitors
AU Eyal, Sara; Yagen, Boris; Sobol, Eyal; Altschuler, Yoram; Shmuel, Miriam; Bialer, Meir
CS Department of Pharmaceutics, School of Pharmacy, Faculty of Medicine, Hebrew University of Jerusalem, Israel
SO Epilepsia (2004), 45(7), 737-744
CODEN: EPILAK; ISSN: 0013-9580
PB Blackwell Publishing, Inc.
DT Journal
LA English
AB Purpose: Valproic acid (VPA), one of the widely used antiepileptic drugs (AEDs), was recently found to inhibit histone deacetylases (HDACs). HDAC inhibitors of a wide range of structures, such as

hydroxamic acids, carboxylic acids, and cyclic tetrapeptides, have various effects on transformed and nontransformed cells, including neuromodulation and neuroprotection. The aim of this study was to assess comparatively the activity of traditional and newer AEDs as HDAC inhibitors. Methods: After incubation of HeLa cells with the tested AEDs, histone hyperacetylation was assessed by immunoblotting with an antibody specific to acetylated histone H4. Direct HDAC inhibition by AEDs was estd. by using HeLa nuclear ext. as an HDACs source and an acetylated lysine substrate. Results: We found that in addn. to VPA, topiramate (TPM) inhibited HDACs with apparent Ki values of 2.22 .+-. 0.67 mM. Although levetiracetam (LEV) had no direct effect on HDACs, its major carboxylic acid metabolite in humans, 2-pyrrolidinone-n-butyric acid (PBA), inhibited HDACs with Ki values of 2.25 .+-. 0.78 mM. The AEDs LEV, phenobarbital, phenytoin, carbamazepine, ethosuximide, gabapentin, and vigabatrin did not inhibit HDACs. The compds. that directly inhibited HDACs also induced the accumulation of acetylated histone H4 in HeLa cells. The effects of TPM and PBA on histone acetylation were significant at 0.25 mM and 1 mM, resp. Conclusions: We found that in addn. to VPA, the newer AED TPM and the major metabolite of LEV, PBA, are able to induce histone hyperacetylation in human cells, although with lower potencies than VPA.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:266919 CAPLUS
DN 140:281367
TI Antibody tools for the diagnostic use in the medical therapy with inhibitors of histone deacetylases
IN Pelicci, Pier Giuseppe; Minucci, Saverio; Piccini, Daniele; Maccarana, Marco; Ronzoni, Simona; Areces, Liliana Beatriz; Faretta, Marco
PA G2m Cancer Drugs Ag, Germany
SO Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1403639	A1	20040331	EP 2002-21984	20020930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CA 2500384	A1	20040408	CA 2003-2500384	20030930
WO 2004029622	A2	20040408	WO 2003-EP10842	20030930

WO 2004029622 A3 20040805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003271663 A1 20040419 AU 2003-271663 20030930
EP 1546712 A2 20050629 EP 2003-753482 20030930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2006501279 T 20060112 JP 2004-539052 20030930
US 20060257948 A1 20061116 US 2005-529792 20051110
PRAI EP 2002-21984 A 20020930
WO 2003-EP10842 W 20030930
AB The invention relates to a method for detg. whether a treatment of a disorder with an histone deacetylases (HDAC) inhibitor is to be started/continued or not comprising detg. the level of histone acetylation in the sample by use of an antibody capable of binding to acetylated histone, and classifying the disorder as to be treated with an HDAC inhibitor when the level of histone acetylation is significantly lower than that of a ref. sample. The invention further relates to the diagnostic and prognostic use of specific antibodies and cell lines producing them.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:533720 CAPLUS
DN 139:195135
TI Changes in histone acetylation during mouse oocyte meiosis
AU Kim, Jin-Moon; Liu, Honglin; Tazaki, Mayuko; Nagata, Masao; Aoki, Fugaku
CS Department of Integrated Biosciences, Graduate School of Frontier Sciences, University of Tokyo, Chiba, 277-8562, Japan
SO Journal of Cell Biology (2003), 162(1), 37-46
CODEN: JCLBA3; ISSN: 0021-9525
PB Rockefeller University Press
DT Journal
LA English
AB We examd. global changes in the acetylation of histones in mouse oocytes

during meiosis. Immunocytochem. with specific antibodies against various acetylated lysine residues on histones H3 and H4 showed that acetylation of all the lysines decreased to undetectable or negligible levels in the oocytes during meiosis, whereas most of these lysines were acetylated during mitosis in preimplantation embryos and somatic cells. When the somatic cell nuclei were transferred into enucleated oocytes, the acetylation of lysines decreased markedly. This type of deacetylation was inhibited by trichostatin A, a specific inhibitor of histone deacetylase (HDAC), thereby indicating that HDAC is able to deacetylate histones during meiosis but not during mitosis. Meiosis-specific deacetylation may be a consequence of the accessibility of HDAC1 to the chromosome, because HDAC1 colocalized with the chromosome during meiosis but not during mitosis. As histone acetylation is thought to play a role in propagating the gene expression pattern to the descendent generation during mitosis, and the gene expression pattern of differentiated oocytes is reprogrammed during meiosis to allow the initiation of a new program by totipotent zygotes of the next generation, our results suggest that the oocyte cytoplasm initializes a program of gene expression by deacetylating histones.

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:346438 CAPLUS

DN 139:111910

TI Involvement of histone acetylation in ovarian steroid-induced decidualization of human endometrial stromal cells

AU Sakai, Nozomi; Maruyama, Tetsuo; Sakurai, Rei; Masuda, Hirotaka; Yamamoto, Yurie; Shimizu, Aki; Kishi, Ikuko; Asada, Hironori; Yamagoe, Satoshi; Yoshimura, Yasunori

CS School of Medicine, Department of Obstetrics and Gynecology, Keio University, Shinjuku-ku, Tokyo, 160-8582, Japan

SO Journal of Biological Chemistry (2003), 278(19), 16675-16682 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB Histone acetyltransferases and histone deacetylases (HDACs) det. the acetylation status of histones, regulating gene transcription. Decidualization is the progestin-induced differentiation of estrogen-primed endometrial stromal cells (ESCs), which is crucial for implantation and maintenance of pregnancy. The authors here show that trichostatin A (TSA), a specific HDAC inhibitor, enhances the up-regulation of decidualization markers such as insulin-like growth factor binding protein-1 (IGFBP-1) and prolactin in a dose-dependent

manner that is directed by 17.beta.-estradiol (E2) plus progesterone (P4) in cultured ESCs, but not glandular cells, both isolated from human endometrium. Morphol. changes resembling decidual transformation were also augmented by co-addn. of TSA. Acid urea triton gel anal. and immunoblot using acetylated histone type-specific antibodies demonstrated that treatment with E2 plus P4 significantly increased the levels of acetylated H3 and H4 whose increment was augmented by co-treatment with TSA. Chromatin immunopptn. assay revealed that treatment with E2 plus P4 increased the amt. of proximal progesterone-responsive region of IGFBP-1 promoter assocd. with acetylated H4, which was dramatically enhanced by co-addn. of TSA. Taken together, the authors' results suggest that histone acetylation is deeply involved in differentiation of human ESCs and that TSA has a potential as an enhancer of decidualization through promotion of progesterone action.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:83868 CAPLUS

DN 138:253482

TI The effect of oxidative stress on histone acetylation and IL-8 release

AU Tomita, K.; Barnes, P. J.; Adcock, I. M.

CS Thoracic Medicine, Imperial College School of Science, Technology and Medicine, National Heart and Lung Institute, London, SW3 6LY, UK

SO Biochemical and Biophysical Research Communications (2003), 301(2), 572-577
CODEN: BBRCA9; ISSN: 0006-291X

PB Elsevier Science

DT Journal

LA English

AB Acetylation of histone residues regulates the expression of inflammatory genes and is controlled by the activities of histone acetyltransferases (HAT) and histone deacetylases (HDAC). Anal. of histone acetylation in human cells is limited by the large nos. needed to perform activity assays or Western blotting. We have used flow cytometry to investigate changes in HAT and HDAC activities at the single cell level and to investigate the effect of hydrogen peroxide (H2O2) on histone H4 acetylation and cell-cycle progression. Using an anti-acetylated histone H4 antibody we show that H2O2 induced a time-dependent increase in histone acetylation that was maintained for 12 h. This was assocd. with increased IL-8 prodn. H2O2 also affected cell-cycle progression. HAT activity was found to be highest in G2/M and equiv. in G0/G1 and S phases of the cell cycle. These

data show that detection of acetylated histone residues at the single cell level using FACs may be a powerful new tool for the anal. of modulation of cell proliferation and gene transcription.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:868228 CAPLUS

DN 138:362277

TI Inhibitors of histone deacetylase and DNA methyltransferase synergistically activate the methylated metallothionein I promoter by activating the transcription factor MTF-1 and forming an open chromatin structure

AU Ghoshal, Kalpana; Datta, Jharna; Majumder, Sarmila; Bai, Shoumei; Dong, Xiaocheng; Parthun, Mark; Jacob, Samson T.

CS Department of Molecular and Cellular Biochemistry, College of Medicine, The Ohio State University, Columbus, OH, 43210, USA

SO Molecular and Cellular Biology (2002), 22(23), 8302-8319 CODEN: MCEBD4; ISSN: 0270-7306

PB American Society for Microbiology

DT Journal

LA English

AB Inhibitors of DNA methyltransferase (Dnmt) and histone deacetylases (HDAC) synergistically activate the methylated metallothionein I gene (MT-I) promoter in mouse lymphosarcoma cells. The cooperative effect of these two classes of inhibitors on MT-I promoter activity was robust following demethylation of only a few CpG dinucleotides by brief exposure to 5-azacytidine (5-AzaC) but persisted even after prolonged treatment with the nucleoside analog. HDAC inhibitors (trichostatin A [TSA] and depsipeptide) either alone or in combination with 5-AzaC did not facilitate demethylation of the MT-I promoter. Treatment of cells with HDAC inhibitors increased accumulation of multiply acetylated forms of H3 and H4 histones that remained unaffected after treatment with 5-AzaC. Chromatin immunopptn. (ChIP) assay showed increased assocn. of acetylated histone H4 and lysine 9 (K9)-acetyl H3 with the MT-I promoter after treatment with TSA, which was not affected following treatment with 5-AzaC. In contrast, the assocn. of K9-Me histone H3 with the MT-I promoter decreased significantly after treatment with 5-AzaC and TSA. ChIP assay with antibodies specific for methyl-CpG binding proteins (MBDs) demonstrated that only methyl-CpG binding protein 2 (MeCP2) was assocd. with the MT-I promoter, which was significantly enhanced after TSA treatment. Assocn. of histone deacetylase 1 (HDAC1) with the promoter decreased after treatment with TSA or 5-AzaC and was abolished after treatment with both inhibitors. Among the DNA methyltransferases, both Dnmt1 and Dnmt3a were assocd. with the

MT-I promoter in the lymphosarcoma cells, and assocn. of Dnmt1 decreased with time after treatment with 5-AzaC. Treatment of these cells with HDAC inhibitors also increased expression of the MTF-1 (metal transcription factor-1) gene as well as its DNA binding activity. In vivo genomic footprinting studies demonstrated increased occupancy of MTF-1 to metal response elements of the MT-I promoter after treatment with both inhibitors. Anal. of the promoter by mapping with restriction enzymes in vivo showed that the MT-I promoter attained a more open chromatin structure after combined treatment with 5-AzaC and TSA as opposed to treatment with either agent alone. These results implicate involvement of multifarious factors including modified histones, MBDs, and Dnmts in silencing the methylated MT-I promoter in lymphosarcoma cells. The synergistic activation of this promoter by these two types of inhibitors is due to demethylation of the promoter and altered assocn. of different factors that leads to reorganization of the chromatin and the resultant increase in accessibility of the promoter to the activated transcription factor MTF-1.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:831339 CAPLUS

DN 136:320242

TI The role of acetylation in rDNA transcription

AU Hirschler-Laszkiewicz, Iwona; Cavanaugh, Alice; Hu, Qiyue; Catania, Jason; Avantaggiati, Maria Laura; Rothblum, Lawrence I.

CS The Henry Hood Research Program, Sigfried and Janet Weis Center for Research, The Geisinger Clinic, Danville, PA, 17822-2618, USA

SO Nucleic Acids Research (2001), 29(20), 4114-4124
CODEN: NARHAD; ISSN: 0305-1048

PB Oxford University Press

DT Journal

LA English

AB Treatment of NIH 3T3 cells with trichostatin A (TSA), an inhibitor of histone deacetylase (HDAC), resulted in a dose-dependent increase in transcription from a rDNA reporter and from endogenous rRNA genes. Chromatin immunopptn. using anti-acetylhistone H4 antibodies demonstrated a direct effect of TSA on the acetylation state of the ribosomal chromatin. TSA did not reverse inhibition of transcription from the rDNA reporter by retinoblastoma (Rb) protein, suggesting that the main mechanism by which Rb blocks rDNA transcription may not involve recruitment of deacetylases to rDNA chromatin. Overexpression of histone transacetylases p300, CBP and PCAF stimulated transcription in transfected NIH 3T3 cells. Recombinant p300, but not PCAF, stimulated rDNA transcription in vitro in the absence of

nucleosomes, suggesting that the stimulation of rDNA transcription by TSA might have a chromatin-independent component. We found that the rDNA transcription factor UBF was acetylated in vivo. Finally, we also demonstrated the nucleolar localization of CBP. Our results suggest that the organization of ribosomal chromatin of higher eukaryotes is not static and that acetylation may be involved in affecting these dynamic changes directly through histone acetylation and/or through acetylation of UBF or one of the other components of rDNA transcription.

RE.CNT 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT